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HEALTH INSURANCE

Within recent years it has become increasingly clear that some form of Health Insurance is inevitable in Canada. When first confronted with such a prospect one cannot help but wonder why such a scheme is necessary right in the middle of a war. For this reason it has been decided that an outline of the projected scheme should be presented. The sole object of this series of articles which will appear in the following four issues of the JOURNAL is to convey information concerning a scheme under which all of us will probably have to work. The editorial staff has therefore set itself the task of trying to answer any questions you may have on the subject and answers will be included in the JOURNAL to such queries as are presented to the editorial staff or written to Room 107 in the Anatomy Building.

Little accurate information has been placed at our disposal until recently in the matter of what has been done and as to what is projected in the field. During the last year, however, a comprehensive report has been submitted with actuarial backing by the Advisory Committee on Health Insurance.

An effort will be made to convey some of the information presented and the conclusions arrived at in this report following the outline presented below.

Section 1—Health Insurance

(a) History and Development
(b) Object

(c) Importance
(d) Existing Schemes
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Section 1

(a) *History and Development*

Health Insurance is just one aspect of a general social security programme aimed at preventing illness and curing disease and thereby lessening the number of hardships the individual is forced to endure.

This tendency to band together for the common good was seen first when the family was maintained as a unit, then came the tribe and now the state.

The earliest State action recorded for the benefit of the general public was the British Poor Law passed in 1601 for the care of those unable to care for themselves. The development of Guilds related to handicraft trades and Social Guilds were primarily for the mutual aid of their members. Later these dissolved as a result of changing social conditions and political manipulations. These were effectively replaced by organizations termed "Friendly Societies" whose aims were not political but purely social. These survived down to the opening of the present century. With the devolpment of the Industrial Revolution living conditions and hence disease and accident incidence were greatly changed and during the 19th century British factory owners (few with philanthropic ideals) made an effort to care for their employees. Trade unions functioning as mutual aid societies appeared for the first time and when as a result of virtually intolerable conditions the pressure of the mass of labour was felt, the government had to vote monies to these societies.

From these experiments various schemes of social legislation developed. From an administrative standpoint these were of two types (a) unilateral concerned with old age and invalidity, mothers' aid, unemployment, medical assistance and rehabilitation; and (b) mutual assistance types such as workmen's compensation, unemployment insurance, sickness and pension insurance.

From the developmental standpoint these reforms have also pursued two paths, i.e. voluntary and mandatory.

Voluntary plans can be traced to the Roman Empire where "Collegais" developed for the provision of a funeral benefit through contributions made during

the lifetime of the individual. Guilds in England with the added responsibility for sickness are recorded as early as the 13th century but these effectively died out by the beginning of the 18th century. They were replaced by Friendly Societies who by means of annual contributions provided some form of compensation during illness and on death provided a funeral benefit. These were so successful that they survived until the beginning of this century and in point of fact it was their actuarial tables which were used by the British Government in their earliest draft of Health Insurance.

Compulsory plans can be traced as far as the writings of Daniel Defoe who advocated such a system in 1697. John Acland succeeded in getting a Bill introduced into the British House as early as 1787 but it failed to pass. Previous to this two small local attempts were made for the care of Coal Heavers on the River Thames and the River Wear in 1757 and 1792 respectively. One must turn to Germany for the first comprehensive Health Insurance Scheme. By 1845 the German government required membership in provident benefit societies. In 1849 employers were first forced to contribute to their employees' insurance. In 1883 Bismarck, with the frank object of combatting socialism, introduced a scheme for the insurance of all industrial employees against accident and sickness and later this was extended to larger sections of the population. In 1888 his example was followed by Hungary and Austria. An Act of National Health Insurance was passed in England under the sponsorship of Lloyd George in 1911 and became effective after the war. This had been in effect ever since.

(b) *Object*

The immediate aims of such a plan are (a) the prevention of disease as far as possible with improvement of living conditions and proper routine medical care; (b) cure in the form of adequate treatment for any disease or accident. Unlike some such plans, the Canadian version makes no provision for cash benefit for the time lost from work though it is possible that some such plan may develop from the present scheme of Unemployment Insurance.

(c) *Importance*

Two great problems are presented by the great advancement of science and medicine in all directions. First the provision of adequate and modern medical care. This entails careful training of many persons for long periods and increasing specialization means ever-increasing numbers. To this is added the problem of distributing such skilled personnel to all parts of the country. Second is the great cost of such a venture. Medical personnel cannot be turned out like nuts and bolts so that each step-up in the number entails a proportionate decrease in cost. Each man, if he is to be effective, must be carefully trained in expensive schools and suitably supplied with the necessary equipment. To this is added the costs of hospitals and institutions of all sorts, the costs of research and all the other aspects of medicine. The only way such facilities can be placed at the disposal of a small wage earner is to cause the expense to be shared by all.

(d) *Existing Schemes of Health Insurance*

Practically all the major countries in the world except Canada and the United States have adopted some form of Health Insurance.

(i) Canadian Experiments in Health Insurance

British Columbia. In 1936 British Columbia passed a Health Insurance Act which never came into effect.

Alberta. This province too has passed an Act which has not yet taken effect.

Saskatchewan. Under their Rural Municipalities Act (sec. 173, sub. sec. 38) a doctor may be encouraged to settle in a community by grants not to exceed $1,500 or by a salary not to exceed $5,000 per annum.

Manitoba. A stystem similar to that in Saskatchewan is used.

Ontario. It is reported that as early as 1808 doctors had made contracts to care for the entire family for a set fee for a year. The Ontario Medical Association Survey of 1931 showed practitioners of the province on the whole in favour of some form of Health Insurance. Employees' medical services particularly in mining towns have been successful not only in individual treatment but also in the broader aspects of medicine. The Town of Windsor has employed a form of Health Insurance which has a registry of 4,000. The most extensive plan yet attempted has been the Associated Medical Services first developed by the Academy of Medicine in Toronto. This now has 30,000 subscribers. The scheme permits selection of the subscriber's own doctor. Care includes medical, surgical, obstetrical, hospital and nursing care and specialized treatment when called for. Fees are $2.00 per month for the subscriber with the added fee of $1.75, $1.50 and $1.25 for the first, second and third dependents respectively and $1.00 for each additional dependent. The results have been that a total of $1,297,674 have been collected and $1,177,394 have been dispersed with a net working balance of $120,260 indicating that the value of the fee is approximately correct.

Quebec. This province employs a system of bequeathing monies on mutual aid societies.

Maritimes. Hospitalization has been provided for Glace Bay miners and their families for 30c per week per employee. A similar system has been tried at Antigonish where $2.00 per capita quarterly pays all hospital expenses.

Certain efforts have been made by the Dominion Government. As as result of a resolution passed in the House in 1928, a committee was formed whose immediate object was to report on insurance against unemployment, sickness and invalidity. Arising from this report was the Employment and Social Insurance Act which provided for Health Grants to the provinces. Unfortunately this act was declared unconstitutional. Later in 1940, a Royal Commission on Dominion-Provincial Affairs expressed the opinion that medical and hospital services were essentially a provincial responsibility but according to precedent previously set, there is no reason why such services should not receive Dominion subsidy.

Finally, in 1941, as a result of a joint meeting of the Minister of Pensions and National Health, the director of Public Health Services of that Department and The Dominion Council of Health, a study of Public Health was begun. In

this the Department was assisted by the Canadian Medical Association. The result was the formation of the Advisory Committee on Health Insurance which was established by order-in-council on February 5th, 1942. As a result of their effort the present draft bill has been compiled.

(ii) Recent Developments in the United States

The Social Security Act of 1935 does not embody any form of State Medicine. Numerous Bills have been introduced into the various State Legislatures but as yet not generalized Health Insurance Program has been developed. The American Medical Association has consistently opposed any system which permits the government to administer the monies of the profession. They state that they are not opposed to Health Insurance as such but have opposed any plan to date attempted on the ground that it permitted political manipulation in a field they feel should be protected from such inroads. On the other hand the Supreme Court of the United States upheld an indictment against them for interfering with a duly constituted plan for group medical practice.

THE BIOCHEMISTRY OF DIABETES

MICHAEL O. O'SULLIVAN*

Diabetes is certainly an interesting disease from a chemical standpoint. There are so many diabetics, and nearly all of them depend upon chemical data for early diagnosis and control of their diabetes. The chemistry of the body is grossly upset, often before the appearance of symptoms, but fortunately the process is reversible, and with the righting of the chemistry, whether by exercise, diet, or insulin, or by a combination of all three, the symptoms disappear. A full understanding of the underlying metabolism is not absolutely necessary in order to treat diabetes but it does make the work more logical and more interesting. Before discussing the practical side of diabetic chemistry, let us consider briefly the factors which are supposed to govern normal fat and carbohydrate metabolism, and why, in the absence of sufficient insulin, excess acetone or ketone bodies appear in the blood and urine. The older theories covering this phenomenon have been seriously challenged in the last few years.

Carbohydrate and Fat Metabolism

Insulin has to do with carbohydrate metabolism, and carbohydrate metabolism is, in turn, linked in some way with fat metabolism. In fact, it is the abnormal fat metabolism which accounts for the ketonemia of diabetes and which leads to diabetic acidosis. The usual fatty acid is a long, straight-chain, monobasic, organic acid containing about 16 or 18 carbon atoms, and is derived from simple fat hydrolysis which yields fatty acids and glycerine.

According to the old, but classical, theory of Knoop, in the normal person the breakdown of fatty acids takes place in regular sequence by oxidation at the β-carbon atom with the production of a new fatty acid containing two less carbons. Normally this process is carried to completion, but in the diabetic individual, apparently due to inadequate oxidation of carbohydrate, the process stops short at the stage of butyric acid, when the fatty acid chain has been reduced to 4 carbon atoms.

Without control of the diabetic condition and the regaining of the ability to oxidize carbohydrate, abnormal products of the decomposition of butyric acid accumulate in the body. Acetoacetic (diacetic) acid and β-hydroxy butyric acid are probably formed first, and from these acetone results. These "acetone bodies" accumulate in great excess in the blood and body tissues generally, overflowing then into the urine.

On the basis of this theory fat has been called a ketogenic food and carbohydrate a ketolytic food. Diets have been formulated containing carbohydrate in the correct proportions to assist in normal fat metabolism. According to this theory glucose oxidation is the all-important factor without which complete fat oxidation is impossible. Since insulin prevented ketosis, it was argued and eventually assumed that insulin helped to burn glucose and indirectly fat. This conception of the interrelationship of carbohydrate and fat metabolism was metaphorically expressed by many, by such phrases as, "Fats burn brightly in the carbohydrate flame," and so on.

This theory was generally accepted until recently, when it was replaced by an

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entirely different, and I think, a much more satisfactory hypothesis. The experimental evidence, which could not be correlated with the old theory, is fairly complex, but the following are two main objections:

(1) Glucose fed to a severe uncontrolled diabetic resulted in an *increased* ketonemia.—It is conceivable with the old theory that if the diabetic had lost the power to oxidize glucose, that his ketonemia might not be lowered by glucose feeding, but it is inconceivable that it should be raised by it.

(2) Experimentally, it has been shown that although diabetics store less sugar as glycogen than normal individuals, their tissues retain the power to oxidize glucose undiminished. In fact, a group of diabetic rats were shown to oxidize twice as much intraperitoneally injected glucose as a non-diabetic strain similarly injected. The old theory, of course, was practically based on the assumption that diabetics lost their ability to oxidize glucose.

During the past few years, various workers have attacked the validity of the Knoop theory. Stadie, in 1940, held that fatty acids were broken down into 4 carbon "acetone bodies" simultaneously, and that it represented a normal process. Diabetics, he claimed, could oxidize ketones as well as non-diabetics, so that a ketonemia must be a result of a piling up of ketone bodies due to their over-production.

In 1942, Somogyi in St. Louis, added his experimental evidence and developed his theory of fat and carbohydrate metabolism. He enumerated two factors controlling production of ketone bodies in the liver, and two factors controlling their consumption in the extrahepatic tissues. He claimed, with regard to their consumption, that glucose is preferentially oxidized in the tissues—i.e. a high blood sugar favours glucose oxidation, and lowers ketone body oxidation. The ex-

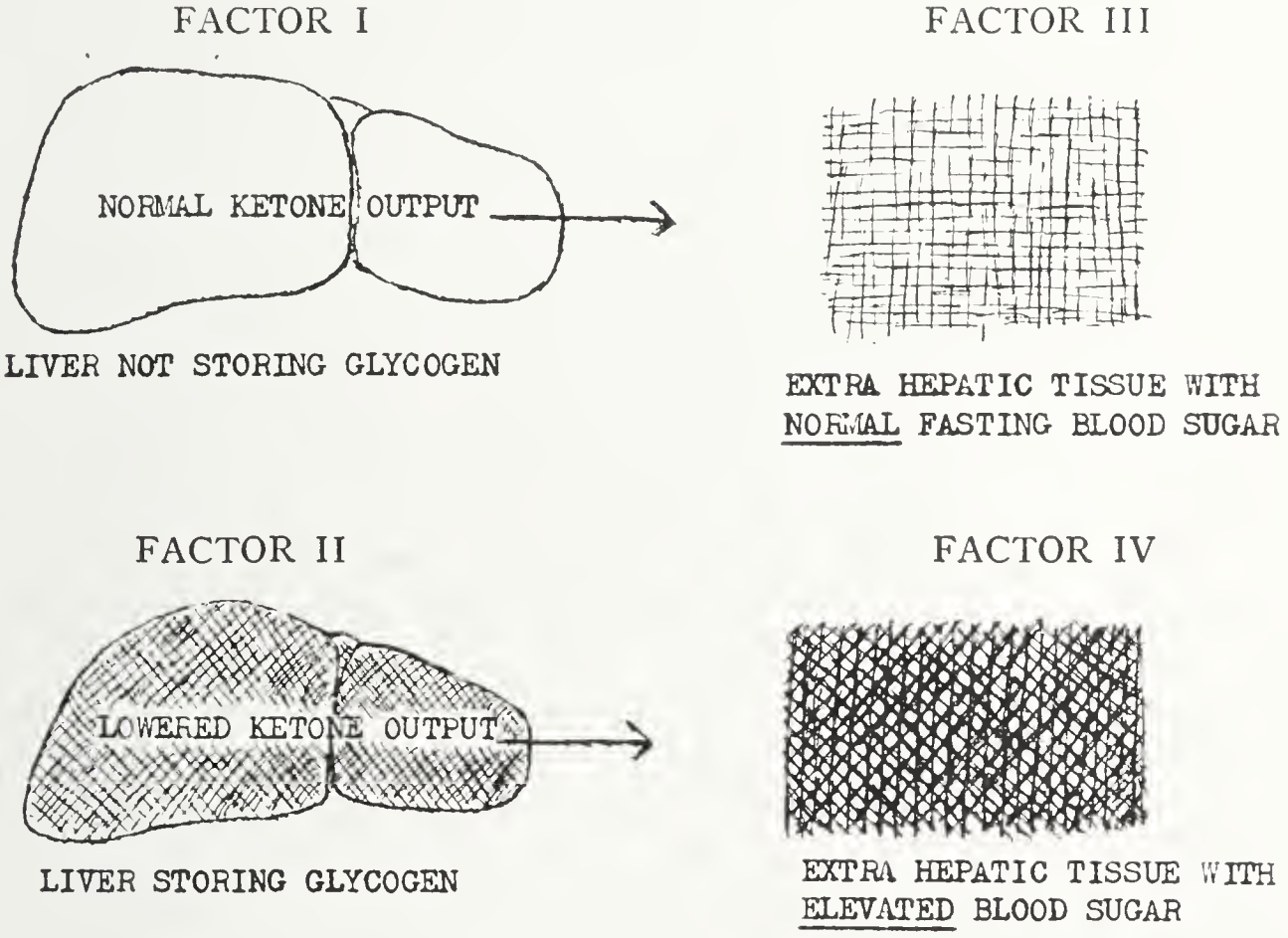

Figure 1

periments with the diabetic rats bear this out. Diagramatically his theory may be represented as in Figure 1. In the normal individual during the post-absorptive period, Factor I is balanced by Factor III—i.e. the production of ketone bodies, although high, is equal to their rate of consumption in the tissues. During the absorptive period, the lowered production in the liver, Factor II, is counterbalanced by the low rate of consumption in the tissues, Factor IV.

In the diabetic individual, Factor I co-exists with Factor IV, since the liver either does not store glycogen, or is continually being deglycogenated, a process which favours even more a high rate of protein and fat catabolism. Meanwhile the abnormally high blood sugars favour glucose rather than ketone body oxidation in the tissues. The administration of extraneous insulin, either by increasing glycogenesis, or by inhibiting glycogenolysis, lowers the ketone body output of the liver and lowers also the sugar in the extrahepatic tissues so that ketone oxidation there returns to normal.

The diabetic acidosis which often accompanies uncontrolled diabetes is rightly blamed on the ketone bodies. Normally there is less than one mgm. percent of these acids present in the blood and their acidic properties do not upset the normal acid-base balance. In severe uncontrolled diabetes however, levels of 100 mgm. percent and even more are not uncommon. The body is capable of withstanding some increase in the content of acetone bodies. Thus a certain portion of ketone acids, because of their weak acid character, can be excreted as free acid in highly acid urine, and another fraction is neutralized by ammonia and excreted. Furthermore, carbon dioxide is displaced from bicarbonate of the plasma by the ketone acids and, by means of this buffer action and that of the blood proteins, considerable amounts of acid can be taken up without appreciable change in the hydrogen ion concentration of the blood. This bodily defense is not, of course, inexhaustible. When excessive amounts of ketone acids accumulate, a certain portion is excreted in the urine along with fixed base, chiefly sodium. This process withdraws elements from the body which can be replaced only from extraneous sources. The reduction of the fixed base of the blood means a reduction in the total salt or electrolyte concentration of the body fluids. To meet this, fluid is excreted with consequent dehydration. The result is lowered body fluid volume with a diminished concentration of base.

Not only are the fixed bases lost in the urine but also there is a depletion of body chloride. This is due in part to the vomiting which is the almost invariable accompaniment of diabetic acidosis, to the marked diuresis which is so characteristic and which is due probably to the effect of the ketone acids, and possibly, in part, to the replacement of the chloride ion by the hydroxybutyric anion and the subsequent excretion of chloride as ammonium chloride. The end results of the above processes are (1) Hemo-concentration and dehydration; (2) Depletion of both fixed base and chloride of the body; (3) Lowering of the CO_2 combining power of the plasma; (4) Shift of the pH of the blood towards the acid side.

The theoretical knowledge which we now possess on this subject may be summarized as follows:

Insulin, a hormone of the pancreas, in conjunction with the liver, aided and abetted by the pituitary, the thyroid, and adrenal glands, regulates the storage of glucose as glycogen in the liver and in the tissues, and thereby maintains the blood sugar at a remarkably constant level. It

was thought for some time that insulin was equally necessary for the oxidation of glucose, but recent experiments do not substantiate this view. When the supply of insulin is inadequate the blood sugar rises, particularly after the injection of glucose or of glycogenic foods. If the supply of insulin is grossly inadequate, or if infection reduces its efficiency, the blood kidneys excrete large amounts of both sugar and ketones, but since the ketone bodies are also acids, fixed base is lost in the process. As mentioned above, the loss of fixed base is followed by acidosis, dehydration, and so on.

Diagnosis

The diagnosis of diabetes is the first

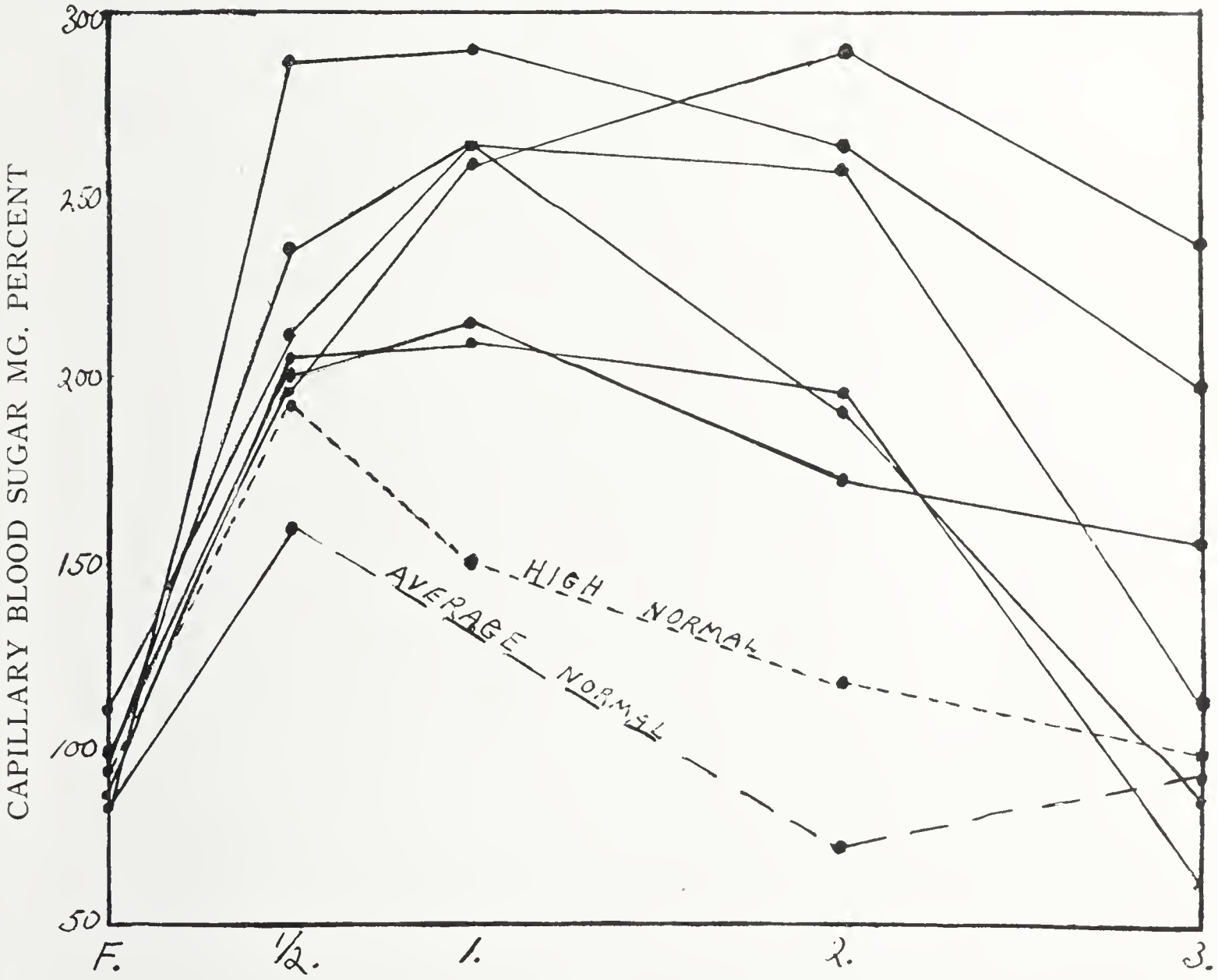

Figure 2

sugar rises to many times its normal value, glycogenesis is markedly reduced, and fat and protein are catabolized to ketone bodies in the liver at a rate which is inconsistent with their low rate of consumption in the tissues. Some of the ketone bodies are toxic and are thought to cause partial or complete unconsciousness by their action on the nerve centres. The practical problem. Early diagnosis is often missed, since, as has already been mentioned, the disease may exist for a time without any clinical signs whatever. Life insurance companies, as a group, are perhaps the most diligent searchers, and everyone knows how dependent they are upon chemical methods to discover latent diabetes. What chemical findings then are

diagnostic of diabetes? First, glycosuria must be present, particularly in relation to meals. In addition, the blood sugar must be either 130 mgm. percent or higher, fasting, or 170 mgm. percent or higher at some time during the absorptive period. If the diabetes is very mild the fasting sugar is nearly always normal and it may save time to run a sugar tolerance test in order to obtain a sugar above 170 mgm. percent with co-existent glycosuria. If hyperthyroidism is a factor these figures must be raised to 150 fasting and 200 post prandial.

It is embarrassing to diagnose diabetes erroneously, and no less serious to fail to show the existence of the disease where it is present. Here are the main pitfalls in connection with the interpretation of chemical data:

(a) Never diagnose diabetes on finding sugar in the urine without blood sugars to establish the diagnosis, for three reasons:
  (1) There are occasions when normal persons show traces of sugar in urine.
  (2) Non-sugar reducing substances sometimes give a false positive with Benedict's solution.
  (3) There are people with low kidney thresholds, the so-called renal glycosurics.

(b) Never rule out diabetes on the ground that a fasting blood sugar is normal. In Figure 2 are given some actual sugar tolerance curves experienced at St. Michael's Hospital over a three months' period. The determinations were made on capillary blood by a method which gives normal values of from 70-95 mgm. percent. These curves, which form a good percentage of the curves run during that period, have been chosen because of their low fasting sugar values. The diagnosis of diabetes was made since glycosuria was present in every case.

(c) Always use fresh blood or blood that is well mixed with fluoride. Glycolysis may cause the sugar in blood to drop 50% in three hours at room temperature.

(d) Do not allow smoking during a sugar tolerance test or attempt to interpret a curve made with an infection present.

(e) There is enough evidence to show that carbohydrate tolerance is definitely influenced by previous diet. Persons who abstain from carbohydrate for days before taking a tolerance test for a life insurance company unwittingly prejudice their case unfavourably.

(f) When capillary blood is used caution must be exercised, since it has been shown that while it is usual during the absorptive period to find capillary-venous differences of the order of 20 mgm. percent, differences of 80 mgm. percent have been recorded. There is no appreciable difference in fasting blood.

A series of 54 capillary blood sugars taken on 54 different normal persons between 2 and 2½ hours after breakfast, gave an average value of 92.7 mgm. percent, with a range of 75 to 109. The standard deviation was 8.16 and the standard error of the mean was 1.11. From these values it was calculated that only one normal person in a hundred would have, by chance, a blood sugar below 67 mgm. percent, or above 119 mgm. percent, between 2 and 2½ hours after an average breakfast.

(g) Due consideration must be given to the method used for determining the blood sugar. The usual Folin-Wu

method gives a normal fasting value averaging 100 mgm. percent. This is known to contain about 20 mgm. percent of non-sugar reducing substances. At St. Michael's Hospital we use a method in which the average normal is about 80 mgm. percent. With this method a fasting sugar of 110 mgm. percent is definitely suggestive.

Treatment

If diagnosis is the first practical problem, control of diabetes is certainly the greatest. When diet, insulin and exercise are properly balanced, the urine is sugar free. If insufficient insulin is available at any time during the day the urine will show sugar at the first voiding made after that time. It should be remembered that urine sugar determinations do not represent the state of diabetic control at the time of voiding, but rather the average amount of sugar spilled since the last micturition. I believe that the urine should be tested just before each meal and upon retiring. If the diet or the insulin dose or both are being shifted from day to day, 24 hour quantitative specimens of urine should be saved and examined quantitatively for sugar and the amount of sugar in grams recorded each day. Meticulous care in the collection and examination of diabetic urines means a lot of work for someone, but I am convinced that their value is far above that obtained even from frequent blood sugar determinations. After all, a blood sugar gives only the condition at the moment, and tells practically nothing about the hours preceding or following it. Why then should blood sugars be used at all to control diabetes? There are two reasons. In a few cases, particularly when they are first seen, all, or nearly all the urines may show a four plus sugar. A blood sugar taken at this time will give approximate information regarding the initial dose of insulin. It might be noted here that the sugar tolerance test is purely a diagnostic procedure and should never be used to judge the severity of the diabetes or to estimate the insulin that will be required.

All other blood sugar determinations should be performed to guard against an overdose of insulin and to watch for improvement of the diabetic condition which usually follows successful control,—i.e. they should be taken when the urine is sugar free, or almost sugar free, and is no longer serving as an index of the unmetabolized sugar. If Protamine Zinc Insulin is used fasting sugars serve as a guide as to how much Protamine Zinc Insulin may be prescribed without the dangers of insulin reactions during the night or in the early morning. If standard or crystalline insulin only is used a fasting sugar will indicate whether or not a small injection is required upon retiring. The greatest use should be made of sugars taken 2 or 3 hours after meals, if and when the urine is sugar free. By these sugar values, threatening reactions during the day may be largely avoided and the final adjustment of the standard insulin may be made. I believe that it is a waste of time to order blood sugar determinations when the urine indicates an excess of sugar unless, of course, one is trying to locate the whereabouts of a patient's renal threshold. So often the laboratory receives an emergency call to come and do so and so's blood sugar because their urine has been showing four plus sugar for some hours. These determinations can only supply information already known, namely, that the patient's blood sugar is high and that he or she needs "quick" insulin at once. Finally, many disturbing blood and urine sugar reports

will assume a more significant meaning if it is remembered that changes in diet and insulin *will not* be reflected in the chemical condition of the patient on the following day or even on the next. The full weight of a change in the doseage of Protamine Zinc Insulin will not be felt for at least three days, and sometimes, for as much as a week. Diets prescribed, and diets eaten, are two different things. Don't forget that actual experiments have shown that diets consumed and diets metabolized are also two different things. The effect of a change in diet may take several days to manifest itself.

Even with the greatest care insulin reactions are not entirely unavoidable. Reactions in the early morning are usually due to protamine Zinc Insulin and it is often necessary to treat them repeatedly with glucose since they may recur for some hours. Reactions due to standard insulin occur about five hours after the administration of the insulin, and may be relieved by a single dose of sugar, usually in the form of orange juice, or as intravenous 50% glucose. The only constant manifestation of insulin shock is a low blood sugar, and for this reason, a blood sample for sugar determination should be obtained before carbohydrate is given. The carbohydrate will do no harm in the meantime but the result of the sugar estimation will cause many a diagnosis to be reviewed. It has been said, wisely, that any sudden "queer" behaviour on the part of a diabetic patient should suggest insulin reaction. Obviously, sugar in the first voided specimen cannot safely rule out a low blood sugar.

Diabetic Coma

Diabetic coma is the unique complication of diabetes. I have already discussed the chemical and metabolic factors which bring about diabetic acidosis and coma. In its early stages this picture of deranged body chemistry may be checked by the timely administration of insulin. However, the onset of coma is so insidious, especially in children, that the patient is often beyond helping himself before the condition is recognized.

No one has a better right to speak out on the treatment of coma than Dr. Joslin of Boston. In the last 20 years he and his associates have treated over 500 cases, and quite recently he has published in the *Journal of the American Medical Association* a series of 62 consecutive cases* without a single fatality.

Diabetic coma has been defined by Dr. Joslin for purposes of comparison with other methods of treatment as a state of diabetic acidosis in which the plasma CO_2 content is 20 vol. percent or less.

Diabetic coma is primarily a deficiency state and no ancillary measures, no matter how helpful in themselves, can ever take the place of insulin. Before the discovery of insulin all acidosis cases whose plasma CO_2 was 20 vol. percent or less died. Frequent blood sugar determinations (and by frequent I mean every hour for the first few hours) should be done in order that large enough doses of insulin will be given early enough. One cannot afford to wait several hours to see if prescribed insulin doses are going to benefit the patient. If the blood sugar does not respond in the first hour the dose must be increased until it does respond. The literature contains reports of many cases in which the insulin requirements during the first 24 hours were over 1,000 units. One of our recent cases at St. Michael's, a boy 8 year's old, required 840 units in the first 12 hours. Another patient required 850 units in 8½ hours to bring

*I have been informed by personal communication that this series did not end until the 85th case, a truly remarkable record.

the blood sugar from 960 to 300 mg. %. Only frequent blood sugars can indicate such a need in time to be of any use. It is quite true that, occasionally, clinical improvement does not follow chemical improvement, but I think it is safe to say that without chemical improvement there can be no clinical improvement. It is very convenient if these serial blood sugar determinations can be made on capillary blood. At St. Michael's, we take pride in the fact that all our blood sugars are determined on capillary blood. Most of our patients nowadays can be diagnosed and controlled without having had a single venipuncture. Many diabetic veins are thus spared for a time when they may be badly needed.

Next to insulin, the greatest need is for intravenous saline. Not only does the rapid and continuous infusion of saline replace the salt and water which has been lost from the body, but it helps to insure the continued functioning of the kidneys. Virtually hundreds of grams of ketone bodies can be passed in a few hours if the urine flow is copious. Some workers still use intravenous glucose as part of their initial treatment of coma. From a chemical view point, I cannot help but agree with Joslin, who stands against its use, on the grounds that: (1) There is already an excess of glucose in the body, (2) And most important, the very valuable and absolutely necessary information obtained from serial blood sugars is nullified if glucose is being added to the circulation. Of course, when the blood sugar has been lowered to the normal level, intravenous glucose should be started, not only to avoid insulin shock, but in order that glycogenesis may continue with the consequent suppression of ketone body formation.

Other helpful measures, such as gastric lavage, cardiac stimulation, etc., are important from a medical standpoint. The use of alkalies is rarely recommended nowadays, as in almost every case insulin and saline by themselves bring about a prompt alleviation of the acidosis.

The prognosis, on admission, is not indicated by any single clinical or laboratory sign. Rabinowich, in Montreal, has constructed a severity-index chart in which the following factors are noted on admission, evaluated, and summed: age, duration of coma, degree of unconsciousness, presence of coffee-ground vomitus, presence of infection, blood pressure systolic, plasma CO_2, blood urea nitrogen, and associated conditions. Notice that the blood sugar is omitted. It is definitely of no prognostic value. Recoveries have taken place frequently with admission blood sugars over 1,000 mgm. percent. Of all the laboratory findings the plasma CO_2 content is most nearly proportional to a favourable prognosis. The admission N.P.N. or urea nitrogen is of little value and is usually a feature of the dehydration. However, a rising N.P.N. several hours after initiation of treatment is an evil omen.

The adequate treatment of severe diabetic acidosis requires the twenty-four hour co-operation of the medical, nursing, and laboratory staffs, but a coma case deserves no less than this. It should be the aim of, and a matter of pride with, every hospital to abolish deaths from diabetic coma completely. If it can be done in Boston, it can be done here.

HEADACHES—PART I*

MECHANISMS AND DIAGNOSIS

W. T. CLARKE, 4T4

This paper is an endeavour to aid in one of the most interesting problems in diagnosis—the patient whose chief complaint is a headache. It is felt the best approach is through an understanding of the causes and underlying mechanisms. For this reason, the arrangement will not be entirely on the basis of the classification proposed for purposes of diagnosis. Instead one part will be devoted to types in which much recent work has been done in order that they may be considered with this work.

Plan

Part I—Recent observations and types of headache they explain.

(a) Anatomical and surgical investigations regarding pain mechanisms.

(b) Experimental observations with histamine and possible applications.

(c) Observations on migraine and related types of headache.

Part II—To be outlined when commenced.

Definition: Any definition of pain is artificial. The point that must be made is that headache is pain from the region of, in general, the head, above the eyes or behind the ears. It is not some peculiar thing.

Pain Paths and Sensitive Sites: The two methods of investigating pain mechanisms are anatomical dissection and physiological experimentation including clinical observation.

*This is the first of two papers on headache presented before Alpha Omega Alpha Fraternity on May 3, 1943, at the home of Dr. Fletcher McPhedran.

Anatomical studies of intracranial innervation were carried out by McLaughlin and Penfield that verify many previous studies. They used a technique of stripping free the dura and nerves in cadavers and in the Macacus Rhesus monkey and then treating with a special neurophilic stain.

The anterior fossa and both surfaces of the tentorium plus related sinuses have a sensory supply from branches of the first division of the trigeminal and the middle fossa is supplied by the maxillary and mandibular divisions. Numerous observations in experiments during intracranial operations under local anaesthetics and with various nerves sectioned verify these routes.

In the posterior fossa the anatomical branches were found to come from the Vagus (X), possibly also from the Glossopharyngeal (IX), and in a small area about the hypoglossal canal perhaps from this nerve.

Stimulation experiments, however, show that the routes are cranial nerves IX and X and cervical nerves 1, 2 and 3. There is a difference as yet between the anatomical explanation and the experimental observations.

A sympathetic vasoconstrictor supply to the cerebral vessels has been demonstrated. Anatomical investigation shows many routes for the cerebrum about intracerebral vessels, ependyma, choroid plexus, and pial vessels connected with most of the cranial nerves. As their nature, whether afferent or efferent is unknown, they are at present of no significance.

There have been found to be six

methods of causing pain from the regions in which headaches are located, and such pain is interpreted as headache most often.

1. Traction on cerebral sinuses or the veins to them.
2. Traction on the middle meningeal artery.
3. Traction on large arteries at base of brain.
4. Distension of intra and extra cranial arteries.
5. Direct pressure on cranial or cervical nerves from the head containing pain afferents.
6. Inflammation about any of the pain sensitive structures of the head (intra or extra cranial).

Intracranial Lesions: It is opportune on this basis, to mention the case of intracranial masses, post traumatic headache, and headache after lumbar puncture.

The presence or absence of headache in *brain tumors* does not correspond to the presence or absence of raised intracranial pressure. Since the cerebrum and leptomeninges are insensitive to stimulation of any type tried, there is no mechanism for oedema or for a mass to produce pain from these structures. The logical explanation is that it is due to traction or pressure on the pain sensitive structures previously outlined. This also explains the inconstant effect of raised intracranial pressure, it depends whether it is uniformly increased or uneven causing displacement of the brain and traction on its vessels. The traction may be local or distant. The pain is of greatest localizing value when it is constant and there is no papilloedema. Oedema, for example as in alcoholism, would be governed by the same considerations. Another type that is explained in this way is that due to subarachnoid haemmorrhage.

Penfield believes adhesions in the subdural space cause *post traumatic headache*. It is easy to understand how these could cause traction on pain sensitive dural sites. He has had success treating cases of breaking down such adhesions. Others believe a persistent chronic oedema accounts for it and they treat it on this basis. Ross, studying post traumatic head pain clinically, has found that a large number of these people have unstable peripheral vascular mechanisms. A very large number have a personality defect sometimes accentuated in the post traumatic period and in other cases apparently arising *de novo* at this time. It would appear that there is more than one factor in different cases, and that perhaps a combination of an intrinsic (personality) and an extrinsic basis is required before the chronic post traumatic headache can occur.

Headache following *lumbar puncture* appears to be caused by traction on pain sensitive structures by which the brain is anchored to the cranium. The fluid withdrawn, or that which subsequently oozes through the hole in the dura (hence the advisability of a small bore needle) causes a fall in cerebrospinal fluid pressure. This allows intracranial venous dilatation and the brain increases in volume. These two factors augment the constant sag of the brain so that it pulls hard enough to cause pain. Pressure on the jugulars as in the Queckenstedt test increases the pain. Tilting the head so as to decrease traction yet not greatly alter the intracranial pressure alleviates the pain. Intra-thecal injection of saline restoring the pressure also alleviates the pain.

Histamine Headache: As headache is so often purely subjective, it was for a long time very difficult to approach

scientifically. Many workers using histamine to investigate circulation time, found they developed a terrific headache.

Direct observation has shown that the large arteries at the base of the brain dilate during the headache brought on by histamine given intravenously. These arteries give the headache if injected with histamine directly. It is relieved by compression on the external jugular veins apparently increasing intracranial pressure and giving support to these vessels. The nerve pathways that must be intact are the Trigeminal, the pain being felt frontoparietally, and cervical 1, 2, and 3, the pain being felt occipitally. Section of the VII or IX cranial nerves does not prevent it. Ligation or anaesthesia of scalp vessels does not prevent it nor does injection of them with histamine cause it.

Clinical headaches that appear related to the histamine type are:

1. Those due to toxemia.
2. Erythromelalgia (to be further described).
3. Those due to vasodilators, e.g. amyl nitrate, carbon dioxide.
4. Those due to foreign proteins.

People subject to chronic headache or migraine are found to have a lower threshold for histamine headaches than those characteristically free of both of these complaints.

Erythromelalgic Headache is a recently described type of headache. Probably extremely uncommon, it is nevertheless quite interesting because it appears to be a specific entity and to have a specific treatment. It occurs in people over fifty, is unilateral, and associated with it are signs of cervical sympathetic involvement — lacrimation, flushing, "stuffiness" of the nostrils. It comes and goes suddenly, often waking the patient at night to be relieved by sitting up. It does not show a familial tendency and there are no aurae. Histamine will cause an attack in those subject to it.

Migraine: An excellent description of this distinct clinical entity with illustrations, and by a doctor who suffered from it himself, is to be found in Allbutt and Rolleston's text. The important fact is that it is a disease entity, a paroxysmal headache that always starts on one side and usually is confined to that side. First attacks usually occur in young people. It is characterized by symptoms appearing in other parts of the body, examples of which are: prodromal depression and mental lassitude; euphoria; scotoma; light illusions—the so-called scintillating fortification figures; or nausea and vomiting (usually towards the end). It shows a marked hereditary tendency, and in this is related to the exudative diatheses or allergies.

Early observers had noted the flushing of the face accompanying an attack of migraine, and even that manual compression of the temporal artery decreased the headache (only as long as the compression was continued).

Wolff devised a method of measuring the pulsations in the branches of the external carotid artery and found they varied as the pain. Also the pain varied as the pulsations when the latter were altered by manual compression or by drugs. Further he showed that experimental distension of the temporal artery caused pain.

Investigations revealed that there was no increased pulsation of the cerebrospinal fluid during an attack of migraine, nor was the pain affected by measures raising the intracranial pressure to support intracranial vessels. Measures relieving the histamine headache do not stop an attack of migraine and vice versa. This and further direct observations show the

ultimate mechanism in migraine is a dilatation of branches of the external carotid artery only.

If this is the ultimate source of the migraine pain, what brings it into action? As is probably true for many ailments, the individual must first of all be susceptible; this is probably the factor giving the high hereditary incidence. Given a susceptible individual there appear to be three important groups of precipitating factors and different ones will be concerned in different cases.

1. *Psychogenic.* A higher incidence of people prone to develop undesirable emotional states, is found in those who have migraine. Personality features, life situations, and emotional reactions all may be involved in the onset of attacks. In a detailed investigation of fourteen cases, twelve had frequency of attacks reduced by an effort to deal with their mental problems. Note the reciprocal relation. Purely mental factors will precipitate an attack in those subject to migraine, and migraine is very liable to cause unhealthy mental states in its victims.

2. *Endocrine.* (a) The condition is about twice as common in the female, in whom endocrine disturbances are thought to be much commoner. (b) It usually comes on about puberty, often ceases during pregnancy and at the climacteric, and the attacks may bear a constant relation to menstruation. (c) Changes in sex hormones in the urine with attacks have been demonstrated.

3. *Food.* The presence of pylorospasm during attacks of migraine has been demonstrated. The ingestion of fat about the time the subject is due for an attack can apparently cause sufficient pyloric tonus to set off the whole autonomic mechanism precipitating the attack.

The close association of allergic phenomena with migraine, and the apparently wonderfully successful results of allergy treatment, have led to many claims that migraine is one manifestation of allergy. However, just as good results have been claimed for many absurd treatments where the only possible value could have been psychogenic. It has yet to be shown that migraine and allergy are not both manifestations of some intrinsic hereditary defect in the individual.

Migraine appears to be a manifestation of vascular instability in which both constriction and/or dilatation may occur in several possible locations, and be precipitated by many different factors.

The same type of investigations as described above indicate the headache in hypertension involves the same vessels as are affected in migraine, only it is usually bilateral. The association of migraine, hypertension and the hypertensive headache suggest some relation, probably genetic. Whatever the exact mechanism of hypertensive headache, over-exertion, fatigue, and mental strain are important factors in bringing on the attacks of pain.

I would like briefly to mention Ophthalmoplegic Migraine, which is not really a type of migraine at all, as it may have a mechanism demanding treatment. It is a severe unilateral head pain that has none of the other characteristics of migraine except ocular signs and symptoms. These include paralysis of one or more eye muscles and diplopia. Cases have been demonstrated due to a leaking berry aneurysm. In these cases, blood is found in the cerebrospinal fluid so this is worth looking for if you ever run across one of these diagnostic canaries.

In Summary:

1. The opening of the cranium under local anaesthesia has brought head pain out of the realm of theories onto a basis of facts.

2. Headaches considered purely mechanical in origin have been described.
3. These improved observations, combined with histamine have aided in the elucidation of the ultimate mechanism in (a) the group we have called the histamine type, related to the internal carotid and vertebral blood supply, and (b) the very important subject of migraine and certain other types described with it, related to the external carotid and its branches.

This provides a basis and stimulation for further investigation; much is still required.

Part II—General remarks on diagnosis with notes on more obscure types.

(a) Classification.

(b) Some common types of headaches not previously considered.

(c) Investigation.

In thinking of any subject, you must have your thoughts organized both for completeness and exactness, hence the value of a *classification.* The simpler and more logical the classification, the more likely you are to remember it. It seems logical to divide all head pain on a basis of origin when you are looking for the cause. Therefore headaches are from (1) local sites, (2) other sources.

In practice, when a patient comes to you complaining of a pain, your first problem is the evaluation of that symptom. Is there an adequate pathological or functional explanation or is it purely a matter of mind? On closer scrutiny this distinction breaks down sadly. If a purely mental pain exists, it may be just as real to the patient as is a child's fear of the dark. Further it is quite probable that the condition of the nervous system has resulted in a functional change that is actually causing pain. Finally, of course, is the probability of a combination of factors. In spite of this the distinction is a worthwhile one when you set out to help the patient get rid of his pain.

The subdivision of the causes in other locations is made on the basis of how they come to be associated with the headache region.

1. Local:
   - (a) pathological or functional
   - (b) psychogenic.
2. Other Sources:
   - (a) neural reference
   - (b) toxic reference
   - (c) vascular reference.

This gives five groups that one should be able to figure out from scratch. I cannot devise a simpler classification.

Psychoneurotic Headaches

The text book features of a psychoneurotic headache are such things as: symptoms continuous days on end, described, not as pain, but as pressure or a band about the head. The description may be in vivid and exaggerated terms. The patients may appear to be emotionally unstable, the headache may be the center of their attention and they are peeved when you dwell on other aspects of their health. It may have been relieved temporarily by many different doctors and treatments.

These are certainly leads if found, however the ideal diagnosis rests on your ability to take such a careful history, revealing the personality vs. environment features that brought on the headache, both to yourself and to the patient, so that he is cured.

In this regard, it must be noted that you do not ask the patient if he is nervous or worried all the time, or he will immediately go on the defensive. You must ask his opinion about things, and determine for yourself his mental state, what

kind of thinking he does, the way his organism adjusts to his environment.

You are limited not only by your own abilities, but also by the patient's intelligence and personality in this difficult problem.

The actual basis of this pain is unknown though it is most likely vascular. An over-readily influenced vasomotor system would cause slight pain in a hypersensitive individual who readily exaggerates this, i.e. the slight actual pain is much worse to him than it would be to others. This purely mental factor which is so exaggerated explains the variations in the pain from that of organic or functional causes. Other authors have suggested spasm of the occipitofrontalis as the source.

Headache in Arteriosclerosis

The only further type of intracranial lesion that will be mentioned is the headache due to cerebral arterial disease. This was found in over 40% of cases diagnosed as cerebral arteriosclerosis (without haemorrhage) in one series. Usually dull, heavy and bregmatic, it may be sharp, stabbing and localized. Hypertension is not a necessary accompaniment. As these people may frequently have senile changes, you may have a tendency to minimize this complaint when they really have pain.

Again the basis is likely vascular. The larger arteries, because of the disease in their walls, fatigue readily so that they become dilated causing pain. However, it is possible that in some cases obliterating disease of the small vessels causes cortical atrophy, giving traction on pain sensitive sites.

Two other locally originating types of headaches are well worth mention—they both arise outside the cranium.

The first has many names, *myalgic, rheumatic, nodular, fibrositic,* etc. Attempts have been made to subdivide this group, but this will not be done here. This pain is nearly always occipital, but may extend to the temporal or even frontal region. Its distinguishing features are: (a) the finding of local tender spots, sometimes even palpable nodules—at the insertion of muscles into the cranium, particularly along the superior nuchal line, and (b) the type of treatment it responds to. It is commoner after 40 years of age, the headache may last through or appear on many successive days, the pain may spread down the neck as far as the shoulders, it is usually made worse by exposure to cold.

The exact cause appears to be a chronic low grade interstitial fibrositis in the muscle and periosteum in some cases, while other types are described in which it is purely a functional disturbance of the muscle. Often there is evidence of low grade infection, such as low fever and increased erythrocyte sedimentation rate; focal infection may be important in some such cases.

Another related, and much commoner type, indeed it may result in the fibrositic type, is *arthritis of the cervical spine.* One should always consider this in occipital pain in those in the proper age group.

Of headaches from distant sources referred to the local area reflexly, the origin may be in the head or elsewhere in the body.

In the head:

Ocular headache: This type is certainly common, so much so that a large percentage of people with headache go directly to the eye doctor. One figure given is that 75% of all bifrontal headaches are ocular. The relation to use of the eyes may make the diagnosis obvious to the patient. Two points in its relation to muscle function are interesting. The

first is that it is much commoner in long-sighted than short-sighted persons, the obvious explanation appears that only the former are using and straining their muscles of accommodation. The second point of interest is that it may arise from the muscles balancing the eyeball movements and that this type is frequently suboccipital. Retinal or optic nerve disease and congestive states about the eye may also cause a headache.

Headache from nasal and nasal sinus pathology; such cases in which the diagnosis is not obvious because of more prominent symptoms related to the infection are over-rated, they are not common. When at this cause it is well to remember the teeth and chronic focal infection anywhere about the head. Unerupted molars is a possibility to be kept in mind.

ORIGINATING OUTSIDE THE HEAD:

The headache of extracephalic origin is notorious, at least in the minds of the laity. Certainly *metabolic disturbances* and toxemias, such as in diabetes, hyperthyroidism, liver disease, gout, etc., can cause headache. There is little good evidence how they do so. The common source they are attributed to however, is the gastro-intestinal tract; commonly *constipation* or even more vaguely, intestinal upset and general fatigue. The theories are just as numerous as they are unproven. It may be that in many the cause is somewhere outside both the gastro-intestinal tract and the nervous system. Some constipated people have a headache which disappears almost at once after a bowel movement. Physiologists have demonstrated the importance of intact nerve connections in the effects of distension of the bowel. This cause must not be ignored as treatment directed towards general body health and morale including the treatment of constipation does help in some obscure cases. I believe it may be the mental impact of a vigorous campaign on the patient plus any improvement in the "tone" of his body and mind that cures the headache, in other words, that they are psychoneurotic.

A fascinating field is that of the *endocrine disturbances.* Chronic headaches other than migraine and related to the menses do occur. Further, it may be relieved by hormone treatment.

Goldzieher has made some interesting observations concerning *salt and water retention* due to which he theorizes a vascular instability which, in the head causes headache. Again acceptance awaits further explanation, observation and the defining of the psychological factors.

Diagnosis and treatment of a headache, as in other medical problems, depends on your experience, on keeping the possibilities in mind, and finally, on having the patience to devote some time to a thorough and intelligently systematic *exposé* of as fascinating a mystery as an "Edgar Wallace". All the specific causes have not been covered; a list of ninety will be found in one of the references and is worth looking over for new ideas. No list of stereotyped questions is given; following this procedure means that you are trying to remember the questions rather than think of the problems and significance of every angle. Such lists are in the references and it is valuable to read them over thinking of the significance of each question.

I think you should take your history on the same basis as in a case of angina pectoris or peptic ulcer, i.e. that there will be no physical findings and therefore the story must be completely diagnostic in itself.

When this is completed it is then imperative to do a physical examination.

In the purely psychogenic cases this is just as important as in organic conditions. Palpation of the head and examination of the fundi are musts. The laboratory investigations are added. Finally you have the therapeutic test for verification of your diagnosis.

An attempt has been made to present some of the interesting features of this difficult clinical problem. Study is best pursued by dealing with actual cases.

The author wishes to thank Dr. Trevor Owen and Dr. Peter Lehman for their suggestions and criticism.

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THE ANXIETY NEUROSES

AETIOLOGY—SYMPTOMS—TREATMENT

STANLEY GREENHILL,* 4T4

"Doctor, I hate to trouble you but I've been so irritable and jumpy and tired recently that it seemed advisable to see you. I'm unable to sleep at nights and it is quite impossible to concentrate on my work. While lately, I've noticed that my heart thumps a lot, and that I easily get out of breath."

It is likely that those of us who go into general practice will be confronted with many such cases. Sometimes the patient may be a fussy, frilly little woman in her middle thirties sitting in an agitated manner on the edge of her chair. Sometimes the tale will be told by an over-anxious mother, acting as spokesman for one of her offspring. Or, again, the patient may be a haggard student in the throes of his final examinations.

Physical examination in cases of this type will seldom reveal anything startling. There may be some physical disturbances of a functional nature—vago-sympathetic upsets shown, for example, by irritability to drugs or by asthmatic attacks that cannot be explained on the grounds of allergy; cardio-vascular symptoms as evidenced by a low cardiac reserve and irregular pulse; gastro-intestinal upsets in the form of unexplained bouts of diarrhoea or constipation, and genito-urinary disorders as shown by frequency of micturition or seminal emission.

It will not take much diagnostic skill to decide that our patient's ill-health is not due primarily to these ephemeral physical disorders but that rather these physical disorders and subjective symptoms are the result of some underlying chronic emotional conflict. Therefore, there is little point in giving our patient a reassuring pat on the back and sending him to the nearest drug-store armed with some hieroglyphics that will tell the pharmacist to give him a nerve tonic. Such therapeutic measures may bring some temporary relief, but the relief is not due to the phosphates or the iron in the tonic but to the inner reassurance brought about by the brief chat in the calm serenity of the doctor's consulting room.

Our patient is suffering from an anxiety state and no amount of drugs, investigations and operations will eradicate the psychogenic factors that are constantly present. In fact, such measures will reinforce these symptoms as the more the doctor becomes concerned with the physical, the more physical pegs the patient will have, upon which to hang the underlying neurosis.

Aetiology

What is an anxiety state? Essentially it is a manifestation of a conflict—a mental conflict that, in its own way, is as real as the physical conflicts we see in every day life. The battle ground in this case is the mind and the warring elements are the instinctual and unconscious cravings of the individual ("ego," "sex," "herd") on the one hand, and the dictates and demands of modern civilization on the other. The tussle is always present even in the most "normal" of us—but that normality was only obtained by our unconsciously following a policy of abject appeasement and compromise in an effort to reconcile these warring elements. A

*This paper was presented to a C.A.M.S.I. clinic group on April 27, 1943.

pyscho-neurosis results, therefore, from an unsatisfactory adjustment between the unconscious desires of the individual and the demands that society makes on him.

From this it can be seen that an anxiety state is purely physchogenic in origin; that often it complicates physical disease and still more often, outlasts it. The presence of physical illness is a boon to the neurotic for here he unconsciously finds an opportunity to give functional expression to his underlying mental conflict and at the same time not give offense to his very sensitive super-ego.

Anxiety states are found more commonly in the female than the male. Though it is impossible to generalize as to the type of individual who is prone to develop anxiety, it is perhaps true to say that the sweet, timid individual, with self-conscious and inhibited mannerisms, who is prone to doubt, indecision and procrastination is potentially an anxiety case. On the other hand, the overbearing, bullying type, who adopts these traits because of an underlying insecurity is likewise liable to develop into a neurotic.

With such an underlying personality, the precipitating factors which may start a train of anxiety symptoms are both innumerable and at the same time often seemingly trivial to a normal individual. The necessity of making an important decision—getting married, leaving home, disappointment in love, sexual irregularities with attendant worry, loss of somebody dear, in fact, fear, worry, conflict of any kind—factors such as these—may be the spark to set off observable symptoms. The symptoms released by these emotional upsets are often regarded as symptoms of serious organic disease, which in itself produces some anxiety, so that a vicious circle of alternating emotional upsets with consequent organic symptoms is set up, and the neurosis may become progressively more involved, with the main precipitating factor buried beneath a pile of secondary emotional disturbances.

The genesis of the physical symptoms in anxiety states may best be understood when it is remembered that any and all functions of the human body are capable of being affected by the emotions through the medium of the autonomic nervous system and the endocrine glands. These physical responses to emotional disturbances are of prime importance in the lower animals, where adequate response may be a matter of life or death. However, these primitive responses have lost their usefulness in our present state of civilization, for more often than not, we are unable to respond naturally to our instincts and instead of giving vent to our emotions we have to divert them to other channels. Most of us are capable of doing this with no ill effects—but there are others who "bottle it up" inside themselves. Finally these "bottled" emotions give evidence of an anxiety state, either mentally, or more commonly, physically.

Symptoms

From the foregoing it can be seen that the physical signs can be manifested in any part of the body. There are, however, some outstanding symptoms of the anxiety state that are worth enumerating—

Insomnia—normally accompanies anxiety. Sleeplessness in itself produces anxiety so that a vicious circle results.

Cardio-vascular symptoms—These take the form of pallor, palpitation, fainting, tachycardia, heart pang—and are due to a prolongation of the normal physical reactions to such things as fear, grief, worry, etc., with consequent setting up a cardio-vascular syndrome.

Respiratory Symptoms—Such common phrases as "it took my breath away," "I

felt breathless," and "I could hardly breathe," indicate that normal emotional stress may bring forth physical symptoms. These are accentuated, prolonged and utilised by the neurotic, with resulting asthma, or attacks of shortwindedness. Like insomnia, asthma in itself produces further anxiety, so that it may become progressively worse and finally chronic.

Genito-urinary symptoms—It is well known that excitement and fear in children often produces uncontrolled passage of urine. So too, in adults, an underlying chronic mental disturbance may bring forth symptoms of polyuria or even incontinence.

Sexual disorders are very frequent in the anxiety state, taking the form of nocturnal seminal emissions, spermatorrhoea, failure of erection, etc., in the male, and frigidity, vaginismus and dyspareunia in the female. These are often associated with fear of "lost manhood," worry over masturbation, conflicts produced by a strict upbringing, unsatisfactory sex relations in marriage, for example coitus interruptus, and premature ejeculation, and countless other causes, all tending to produce fear and worry in the mind of the individual.

Gastro-Intestinal Symptoms — Anxiety may produce dryness of the mouth, anorexia, poor or excess gastric secretion, diarrhoea, and constipation. If such disturbances give rise to the conviction that these symptoms are in themselves manifestation of disease, then the patient will suffer from a functional gastro-intestinal disorder.

Headaches, fatigue,—not consistent with the work performed, phobias, visual disturbances, nasal troubles, tics, etc., may all result from an underlying anxiety state.

Physical Examination

The physical examination should be extremely thorough, not so much because of the information the doctor may obtain from it, but in order that the patient will be aware that nothing has been omitted which might possibly be a source of the trouble. It is also well to remember, that a patient of this type has probably been to several doctors previously in search of a cure, and that by now he is well versed in the ritual of examination. If he has been made to believe that his "overhaul" was slipshod and hurried, he will immediately lose confidence, and the chance to effect a permanent cure will have been lost, before the real treatment has been started.

What should the patient be told in such a case? Don't tell him that he is perfectly healthy, and by the tone of voice infer that he is probably a malingerer or a hypochondriac! He is probably unconsciously deriving benefit from his illness—he feels better when under the charge of a doctor, and obtains some relief from the belief that he is in good hands in the event of further symptoms. If he is told there is nothing at all the matter, great depression will follow, and he will reappear at some other doctor's office with still more disturbing signs. He should be told the truth about the physical findings—namely that the signs of physical disease are completely out of proportion to the signs of any organic lesion. Then explain to him, that in your opinion, these symptoms have all the earmarks of an emotional basis, and that under suitable treatment you feel sure they can be eradicated.

Treatment

With the completion of the physical examination, it is now possible to start making a more direct attack upon the

anxiety state itself. The initial step in this direction is the taking of a full and comprehensive history. Considerable time should be allowed for this all important first interview—at least one hour—for not only has the history to be obtained, but perhaps what is even more important, there has to be established a doctor-patient relationship that combines not only complete frankness on the part of the patient, but also the realization that in spite of these exchanges of innermost thoughts the doctor must remain the doctor and not become the object of the patient's transferred loves and hates. A situation which is quite common, occasionally amusing, and often decidedly alarming.

The history should be detailed, and told almost entirely by the patient. Naturally it will be long and rambling, filled with over-accentuated trivialities, fleeting references to important factors, and complete omission of those happenings that either produce unpleasant thoughts in the patient's mind, or have been completely repressed. Once the patient has unloaded his pile of symptoms, it is advisable, by tactful questioning, to enquire into the environmental factors, and emotional disturbances that occurred at the time of the most recent attack. Often the patient will "forget" or "cannot recall" these happenings, but by encouraging him to remember the bits and pieces of his life around that time the "resistance" will be overcome and a true account be obtained.

The ice has now been broken, and the psychiatrist and patient go over the prominent symptoms together, working out the chronological relationship between their occurrence and emotional disturbances experienced by the patient. Gradually, the factors present at the time of the initial attack of symptoms will have been uncovered. Of course, all this does not imply plain sailing—often there will be complete denial of anything untoward having happened at the time of onset of symptoms, but as the treatment proceeds and the patient's resistance becomes less, these periods of slow going will become rarer.

During this time, the cause and effect relationship between emotion and physical symptoms will be becoming apparent to the patient. Hitherto, these symptoms have either been regarded as manifestations of real organic disease, or as completely unexplainable and annoying phenomena associated with the general "run down" condition. But with the insight gained during the treatment, as well as the explanations given by the psychiatrist, the patient is now able to see the correlation of physical symptoms with periods of emotional stress—and it is this "seeing things for himself" that determines in the long run, whether or not, the treatment will be successful and the cure permanent.

Finally before closing, it might be advisable to give what has gone before a certain air of reality by citing a specific case, and briefly outlining the underlying psychic factors that became apparent during analysis.

The following case is an abbreviated version of one described by Brill. Unfortunately, the most striking symptoms presented by the patient were various types of phobias, a subject to which only fleeting reference was made, but as the case presents many of the salient features so typical of a psychoneurotic state, it is perhaps a fitting epilogue to this very brief resume of an extremely broad subject.

The patient was a 33-year-old drug salesman, who five years previous to treatment had developed a mania for washing his hands. Since that time this mania had expanded considerably, and by the time he was under the care of a psychiatrist, he had developed a phobia for dirt

in any form whatsoever—being afraid to touch anything for fear of contaminating either himself or immediate contacts. He was obviously incapacitated by this obsession and was quite unable to do anything. This phobia gradually developed into a fear of poisons and drugs—he saw poisons everywhere—in the matches he used for lighting cigars, in wet paint on buildings, and in the green rust, which he called "canker", that collected on any metal exposed to the elements.

The history, which went back into childhood, revealed amongst other things, that he had been a "peeping Tom", was an aggressive youth, showed coprophilic tendencies, masturbated before puberty, and became precociously interested in the opposite sex at the tender age of eleven. It was not until he was 21, that definite neurotic symptoms became apparent. At that time he was a scrupulous, moral and conscientious young man, showing a strong attachment to his mother. It can be seen from this that the patient, except for accentuated sexual activities, was upon casual observation essentially a normal individual. There were, however, strong repressions and suppressions present at this time. His father had left him the drug business, a business which had no appeal, but which he felt was his duty to perpetuate. His mother was also aware of this antipathy, but in spite of her counter suggestions he was determined to direct the concern. This decision was greatly influenced by the fact that his mother was seriously ill, and that the other members of the family had given no real evidence of any filial affection. She was constantly urging him to follow the straight and narrow path, in contradistinction to the other members of the family, and this he tried hard to do. However, he ultimately had an affair with some woman—an incident which gave him a feeling of great fear and remorse, as he felt unable to tell his mother about it.

In the meantime she was becoming progressively worse and a few days prior to her death he developed this hand washing habit.

Obviously the patient was leading an unduly repressed life. He was quite unable to find any outlet. The dislike for his work made it impossible for him to sublimate his energies in this direction and the strict moral and religious upbringing prevented his developing into the typical roué. He could therefore find no relief for his repressed energies and so unconsciously he reverted to his childish habits. Such habits were by now quite incompatible with his sensitive ego, and consequently manifested themselves in negative form, and the handwashing became symbolic for the washing away of a moral stain. Generalization and rationalization occurred as would be seen by the fact that he feared all stains, and stains began to represent drugs and poisons. The "canker" of which he was so frightened was found to be a sound association with the word "cancer"—the disease from which his mother died.

During the period of treatment—which lasted five months—the patient gained complete insight into his condition and left completely cured. Later when he came to pay his psychiatrist a social call he mentioned that he had left the drug business, and now was doing well as a seller of perfumes!

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THE JUXTA-GLOMERULAR APPARATUS

R. J. HOLDEN, 4T5

Much has been made lately of the role of the kidney and of renin, a substance derived from renal cortex, in the production of hypertension. It is in regard to the latter substance that one encounters reference to the juxta-glomerular apparatus. It is the purpose of this article to present some of the facts regarding the structure and function of this recently discovered group of cells.

Structure

Although men have been looking at sections of kidney ever since the birth of the microscope, it was not until about 1923 that Goormahgtigh, working in the University of Brussels, recognized and described a hitherto overlooked group of cells. This was the juxta glomerular apparatus. It consists of a cell cluster having a constant morphological relationship to the glomeruli and afferent arterioles in the renal cortex. The cells are disposed in two groups: (1) those which lie in a triangle bounded by the base of the vascular tuft of the glomerulus, the macula densa and the afferent arteriole; and (2) those which lie diffusely in the media of the small renal arterioles. Of the latter group, some cells are arranged eccentrically about the afferent arteriole, which they completely surround, lying in immediate contact with the macula densa of the distal convoluted tubule. Other cells lie scattered in the outer one-third of the media, between smooth muscle fibres of the interlobular and terminal arteries. Still others are found in the walls of the smaller arterial vessels, where they form the entire vascular wall, separated from the lumen only by endothelium.

Structurally, these cells fall into the epithelioid type. They are large, polygonal and rather pale with distinct borders. They are closely packed and have running between them what appear to be non-medullated nerve fibres. The cytoplasm is scanty but looks plentiful, due to the presence of vacuoles; the nuclei are small, round and vesicular. Many of the cells contain fine acidophilic or basophilic granules in their cytoplasm. These are termed afibrillar cells. Of those scattered among the smooth muscle fibres of the renal arterioles, many are seen to contain varying numbers of what are apparently fragments of smooth muscle bundles in addition to the granules. According to the number of fragmentary muscle bundles, these cells are known as fibrillar or paucifibrillar.

Indeed, it is thought that the cells of the juxta glomerular apparatus arise from smooth muscle cells and that the paucifibrillar cells represent the transitional stage between the smooth muscle cells on the one hand and the epithelioid afibrillar cells on the other. These transition paucifibrillar cells are but rarely found in the group at the base of the glomerular tuft, being encountered mainly along the renal vessels.

That there are two types of cell in the walls of the renal arterioles—muscular and epithelioid—can be demonstrated by methods other than histological examination. In experimental animals, it has been shown that small doses of Vitamin D_2 over a period of a few months stimulate the metabolism of the body tissues, and this is reflected by a cellular hypertrophy. Vitamin D_2 or calciferol is produced by the irradiation of yeast, and consists of irradiated ergosterol. In the renal arterioles, Vitamin D_2 acts primarily on the

two cellular components in the media of their walls. As the dosage is increased, the hypertrophy of both muscular and epithelioid cells becomes more pronounced and generalized. However, it is when too large doses are administered for too long a period that differentiation of the two cell types takes place. The smooth muscle cells, after preliminary hypertrophy begin to degenerate, become necrotic and finally hyalinized. The afibrillar cells on the other hand, after preliminary hypertrophy, practically never degenerate and remain as plump viable vacuolate cells lying among the necrotic muscle fibres. Hence, by the administration of sublethal doses of Vitamin D_2, there can be shown a difference in reaction on the part of the two types of cell present in the media, a difference which naturally suggests independent functions of the different cells.

Function of the Apparatus

Theories regarding functions were formulated as fast as new features were discovered. One of the first things noted about the apparatus was its close resemblance to the glomus of the digital arteries. In describing the musculature of the wall of an arterio-venous anastomosis in digital glomerula, one writer says:

"Amid the muscle cells of the wall are seen large clear epithelioid-like cells with oval or globular nuclei which are poor in chromatin. The cells are poor in myofibrils and ramifying about these cells are non-medullated nerve fibres". The juxta glomerular apparatus appears to be almost identical with the epithelioid cells of the A-V anastomosis. By analogy, the identical structures of the two organs suggests a similar function, i.e. the afibrillar cells situated between contractile arteriolar segments and capillary networks must intervene in the eventual exclusion of the glomerular loops from the renal circulation, thus rendering the glomeruli ischaemic.

One German worker thought the epithelioid cells controlled the tone of the musculature of the afferent arterioles and that increased turgescence of them would close off or divert blood from the glomeruli.

The presence of nerve fibres in the juxta glomerular apparatus provided interesting possibilities. Indeed, work was done indicating that a nervous reflex initiated by the afibrillar cells controlled the contracture of the afferent arterioles. It was supposed that this reflex was stimulated by the changes in the composition of the glomerular filtrate as it passed through the macula densa of the distal convoluted tubule (which was found always to be in close relation to the juxta glomerular apparatus situated at the base of the glomerular tuft); and that nervous impulses were conveyed by the nerve fibres to the smooth muscle cells of the arteriolar wall.

According to other observers, the nervous plexus had another explanation. They showed that the heart was not the only part of the circulatory system to possess the property of rhythmical contraction, but that arteries, A-V. shunts, and arterioles had also, to a variable extent, the power of rhythmical pulsation. They conceived the epithelioid cells scattered along the renal vasculature as the homologue of the pale cells of the conducting system of the heart and that just as the S-A. node was the pace-maker of the heart, so the juxta-glomerular apparatus was responsible for the rhythmical "milking" contractions of the renal vessels that had been observed previously.

In all of the above theories, there is a sense of confusion as to the exact function of the juxta-glomerular apparatus. How-

ever, they all have one theme in common, viz., that the apparatus in some way controls the blood supply to the glomerulus.

The Endocrine Nature of the Apparatus

There remained, however, one possibility dear to every physiologist's heart —the possibility that the apparatus might be an endocrine gland. Thanks again to the work of Goorhmagtigh and others, histological evidence of the endocrine nature of these cells has been forthcoming.

These workers have been using dogs and rabbits because in these animals the granules in the epithelioid afibrillar cells are much more prominent than in human material. However, in fresh autopsy specimens of human hypertensives—all cases suffering from chronic glomerulonephritis and nephrosclerosis—changes have been observed, though on a reduced scale, that correspond exactly to the experimental findings in animals described below.

The blood pressure in animals was raised either by the injection of aspartic acid or by Goldblatt's silver clamps. In such hypertensive animals, the most striking feature is a marked increase in the number of the acidophilic cells at the base of the glomerulus and along the vessels. These cells apparently increase at the expense of the basophilic and afibrillar cells of the apparatus for their numbers are decreased in hypertension. Concomitant with the increase in acidophilic cells is an increase in the number of acid granules in their cytoplasm. As the hypertension increases, the hyperplasia of the apparatus is so pronounced that acidophilic cells are pushed along the capillary loops of the glomeruli and obliterate the proximal part of the glomerular space. In extreme cases of high blood pressure, the acidophilic cells decreased in number and showed evidences of hydropic degeneration, indicating exhaustion of the cell comparable to that seen in the β-cells in the islets of Langerhans in the end stages of diabetes. It was noted also that in animals showing a decreasing blood pressure the number of acidophilic granules was reduced. The above illustrations show the close relationship of the acid granules of the juxta-glomerular apparatus to the degree of hypertension.

At this point, it should be explained that the cells of the juxta-glomerular apparatus undergo a progressive cyclic change in hypertensives. Normal smooth muscle cells are converted into paucifibrillar cells with fragments of muscle fibres and then into afibrillar cells with clear cytoplasm. These afibrillar cells are the stem cells of the granular series, and they are found in large numbers even in normal cases. Mitotic figures have only so far been observed in the afibrillar stem cell. In hypertensive people, however, something stimulates these, and they actively multiply and pass through a basophilic stage to the mature acidophilic epithelioid cell. From microscopic evidence, it is only the acidophiles which have the endocrine function of secretion.

Since the work of Goldblatt in 1936, it has been thought that the substance liberated by these cells is renin. Support of this belief is lent by the fact that renin is most abundant in the cortex of kidneys, particularly in hypertensive ones, and that the cells of the juxta-glomerular apparatus are found largely in the renal cortex. The total number of these cells is very greatly increased in hypertension.

Later experiments tend to substantiate the findings mentioned above. However, it must be said here that the whole subject of the function of the juxta-glomerular apparatus is still in the experimental stage,

and no definite conclusions should be formed as yet without further work on the subject. But the thought that many cases of hypertension may be due to endocrine malfunction cannot help but direct one's hopes toward a more hopeful treatment of high blood pressure.

SUMMARY

The histological appearance of the juxta glomerular apparatus is described, and the various theories dealing with the relation of neighbouring structures are presented. The effect of Vitamin D_2 in differentiating the epithelioid cells and muscle cells of the arteriolar walls and the evidence in favour of an endocrine nature of the apparatus is presented. The progressive metaplastic cycle of the cells from smooth to acidophilicy is described.

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—quoted from "Parergon," published by Mead Johnson & Company, Evansville, Ind. Free copy available to physicians on request.

Abstracts

JACK LAIDLAW, Editor

Dieppe in Retrospect

By J. A. MacFarlane
Lancet, April 7, 1943

This is the report of some 600 Canadian wounded who were treated in hospital after the Dieppe raid in August, 1942. The mortality was 2.5%, remarkably low considering that the time between wounding and admission to hospital ranged from 20 to 36 hours.

Medical officers landed with the men but had little time for more than casual first aid and the directing of the evacuation of the wounded from the beaches.

Ninety-two per cent received one or more of the sulfonamides. They were not administered on the beaches but were given whenever possible on the voyage home and on arrival of the casualties in England. Sulfanilamide was the commonest drug used locally while sulfapyridine and sulfathiazole were mainly given by mouth.

There were no cases of tetanus and this was thought to be due to the fact that all Canadian military personnel are actively immunized with tetanus toxoid. At that time the new policy of giving a boosting dose of toxoid to all wounded men was not in operation.

Transfusion with blood or blood substitutes was carried out in 10% of cases, even on small craft intermittently under heavy enemy attack.

Slightly more than half of the wounded required anaesthetic for operative procedures and of these a large proportion received intravenous pentothal sodium. This anaesthetic was found particularly valuable for short operative procedures such as attention to wounds of the extremities.

Head wounds were uncommon; only seven relatively severe cases were reported. In all, fragmented bone, pulped brain and readily accessible metallic bodies were removed, a sulfonamide introduced locally and the wound closed. There was only one fatal case.

There were 16 casualties with penetrating abdonminal wounds, nine of whom subsequently died. The high mortality was believed greatly influenced by the long and difficult journey across the channel.

There were 30 cases of penetrating chest wounds. Of these, 27 survived, the three fatalities having penetrating abdominal wounds as well. The treatment was on the whole conservative, though repeated aspiration was used with good effect in haemothorax.

Twenty per cent of the wounded (117 men) suffered compound fractures. The vast majority of these were caused by metallic fragments of shell or mortar casing, only a few by rifle or machine gun bullets. In spite of the long exposture before treatment (average—32 hours), the condition of these men was remarkably good, less than 10% requiring transfusion at the time of operation. There was gross wound infection in only 15, five showing evidence of gas gangrene. Treatment followed the rules laid down by Trueta: wide exploration and debridement, packing with vaseline or plain gauze, and immobilization in a skin-tight plaster. Sulfonamides were administered locally and by mouth. Osteomyelitis developed in nine cases. Eleven only

required amputation. There were no instances of fat embolism and no deaths.

Soft tissue wounds were likewise explored and excised, and nearly all were left open and packed. After three of four days many of the larger wounds were immobilized in plaster and these men were more comfortable.

There were 13 cases of gas gangrene with only one death. All received radical local excision and immobilization in plaster. In six instances, however, amputation was necessary. No antitoxin was used but sulfonamides were again given locally and by mouth.

The incidence of peripheral nerve injuries was relatively high, the majority associated with compound fractures. In a few cases the nerve ends were brought together with one or two sutures in order that they might be more easily found at a later exploration. Nerve trunks bathed in a high concentration of sulfonamide were found in a number of cases to suffer severe and lasting damage; hence the use of these drugs in wounds with damaged peripheral nerves is not advised. It is also recommened that careful note of sensory and motor loss with subsequent changes be made on a special sheet for the benefit of those making an exploration at a later date.

Abdominal Injuries Due to Underwater Explosions

By G. R. Cameron, R. H. D. Short, C. P. G. Wakely
British Journal of Surgery, July, 1943

In this article the authors deal only with abdominal injuries due to underwater explosion of depth charges, mines, bombs and torpedoes. A description of 20 cases which were subjected to operation is given first, then an analysis of 80 cases which, though severely shocked by the explosions, recovered without operation; in all these instances the men were swimming away from their sinking ships when the under-water explosion occurred.

At the time of the explosion a sharp pain, often described as a "sharp kick," was felt in the back; this was occasionally accompanied by sharp testicular pain later found to be due to small haemorrhages beneath the tunica albuginea. Paralysis of the legs commonly followed; this lasted for an hour or so, then a tingling sensation like "pins and needles" set in until the movements of the legs shortly became normal again. Vomiting was a constant symptom. In all but two of the 20 cases evidence of perforation was present within a few hours; in the two this complication did not occur until the tenth day when the men were up and around again. In no instance were there signs of external injury.

At operation retroperitoneal and subserous haemorrhages were found in all cases. Perforations of the caecum were present in nine, of the ileum in seven, while in four cases there were multiple perforations. The intestinal lesions evidently occurred in those regions of the tract containing a large amount of gas. Solid visiera were rarely damaged and the liver was ruptured in only one case. It was suggested, however, that the liver was probably injured quite frequently in fatal cases. The late perforations on the tenth day after the explosion were believed caused by haemorrhage initiated by the primary injury.

Treatment, other than combatting shock, consisted of closure of the perforation and overlaying it with an omental graft. Ten of the 20 casualties, including the four with multiple performations, subsequently died.

With the 80 cases who were injured by the immersion blast but recoverd without

operation the commonest symptom was abdominal pain which persisted for from three days to three months after the injury. Melaena was present in 82% and in some persisted for four months. Twenty per cent of cases gave a history of hemoptysis while in 14% hematemesis was reported. In only two of 32 cases in which sigmoidoscopy was performed was there any abnormality revealed and in these small scattered petichial haemorrhages could be seen high up on the rectal wall and lower sigmoid; examination a month later disclosed normal mucous membrane. Not one of these casualties showed any sign of external injury. From examination of available records it appeared that cases which recovered from immersion blast very rarely suffered any permanent effects.

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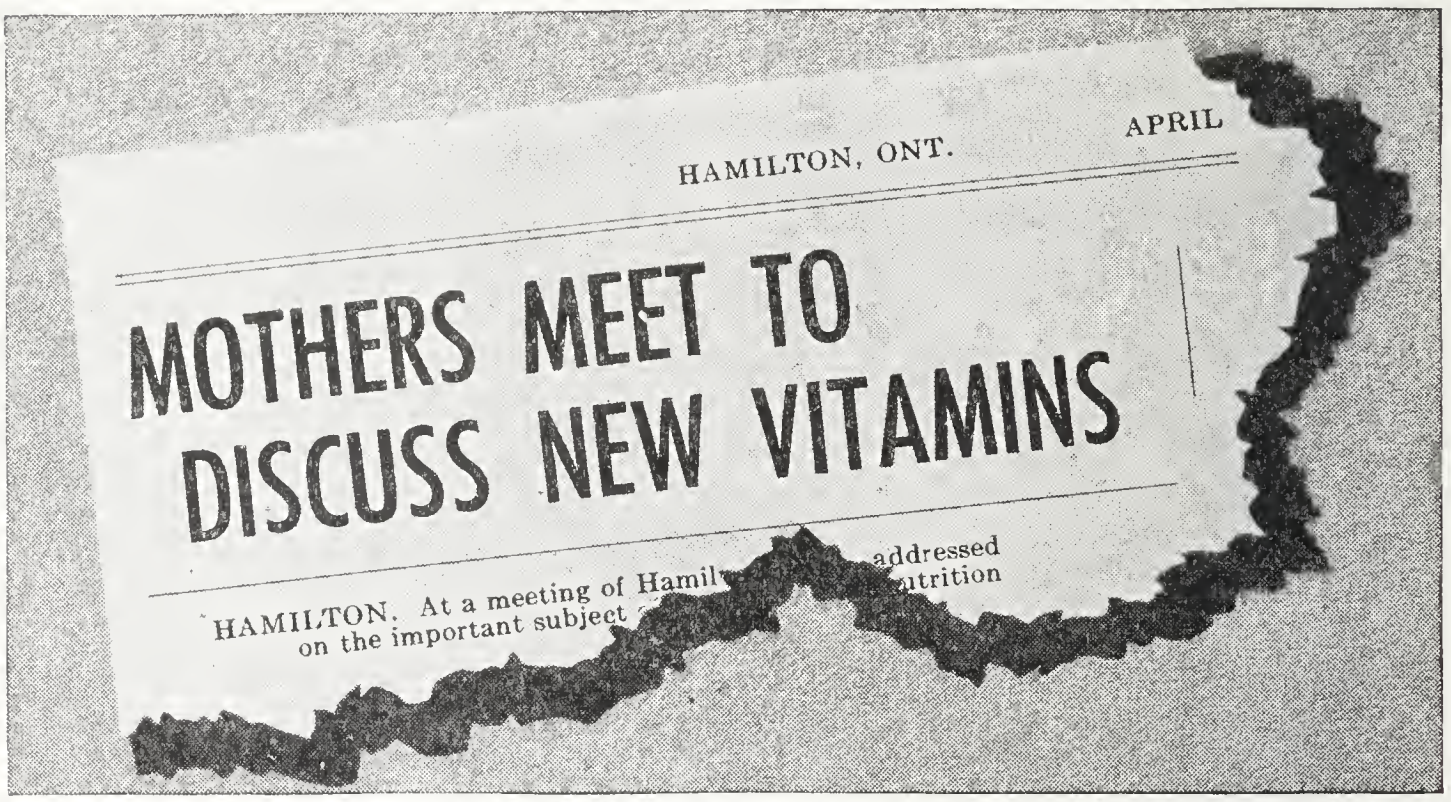
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(1) *What are the Vitamins?*, W. H. Eddy, Reinhold Publishing Corp., New York, 1941.

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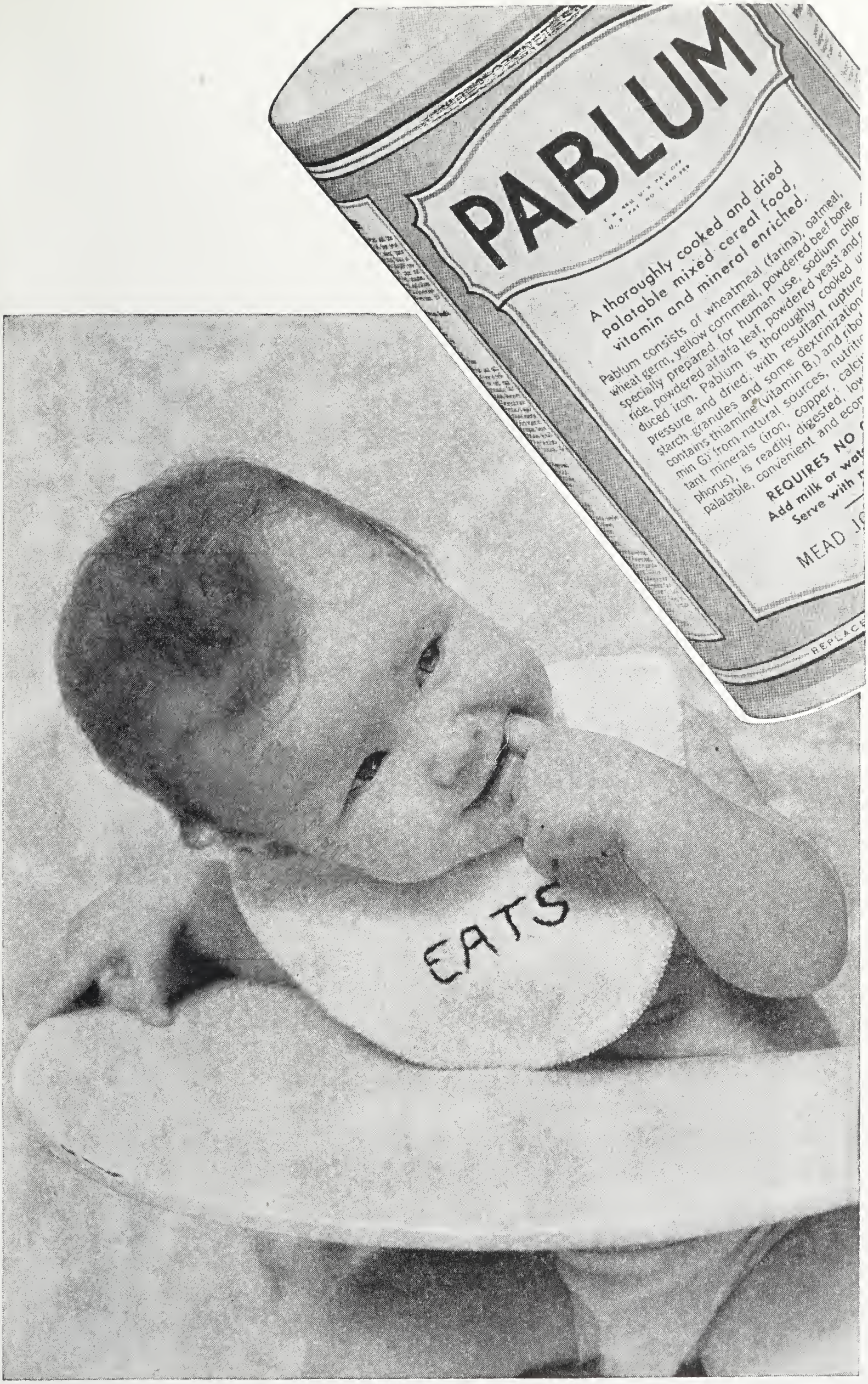
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